REMARKS

Claims 1-5, 8-11 and 14-16 are pending in this application. The rejection of these claims under 35 U.S.C. § 103 was maintained. It is alleged that these claims are obvious over U.S. Patent No. 5,994,069 to Hall *et al.* ("Hall") in view of U.S. Patent No. 6,387,621 to Wittwer *et al.* ("Wittwer"). Applicants respectfully traverse this rejection.

The Patent Office bears the burden of establishing a *prima facie* case of obviousness under 35 U.S.C. § 103. *In re Deuel*, 51 F.3d 1552, 1557 (Fed. Cir. 1995); *In re Rijckaert*, 9 F.3d 1531, 1532 (Fed. Cir. 1993). To establish a *prima facie* case of obviousness, the Patent Office must first show that the prior art suggested to those of ordinary skill in the art that they should make the claimed composition or device or carry out the claimed process. Second, it must show that the prior art would have provided one of ordinary skill in the art with a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be adequately founded in the prior art and not in an applicant's disclosure. Third, the Patent Office must show that the prior art teaches or suggests all the claim limitations. *Manual of Patent Examining Procedure*, § 2143; *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). These criteria must be satisfied with factual and objective evidence found in the prior art: an examiner's conclusory statement cannot form a basis for a *prima facie* case of obviousness. *In re Sang-Su Lee*, 277 F.3d 1338, 1343-4 (Fed. Cir. 2002). Applicants respectfully submit that these criteria are not met by the combination of Hall and Wittwer.

The Examiner correctly recognizes that Hall does not teach the modes of data analysis that can be used to overcome the background problem. However, the Examiner alleges that the pending claims are obvious because: (1) the combination of Hall and Wittwer discloses methods of overcoming the background identical to those recited by the pending claims; and (2) a significant motivation exists because Hall recognizes the background problem and Wittwer states that its algorithms can be applied to any amplification system including exonuclease methods. Office Action, pages 7-8. Applicants respectfully disagree.

Applicants respectfully submit that the combination of Hall and Wittwer does not disclose each and every limitations of the pending claims (*i.e.*, Wittwer does not disclose an analytical methods identical to those recited by the pending claims). The Examiner repeatedly refers to Figure 5 and columns 7 and 8 of Wittwer, and alleges that those portions of Wittwer teach the steps (b) and (c) recited by claim 1. However, Applicants fail to see how the portions of Wittwer referred to by the Examiner disclose these steps.

Referring to Figure 5 of Wittwer, the Examiner contends that it discloses linear behavior of negative signals and non-linear behavior of positive signals. Office Action, page 5. As Applicants previously pointed out, Figure 5 does not show that negative signals exhibit linear behavior: the negative result shown in Figure 5 appears to be a curve obtained from second order kinetics. Furthermore, those of ordinary skill in the art, examining the positive signals shown in Figure 5, had no reason to believe that all positive signals would exhibit non-linear behavior. This is because Figure 5 is a mere illustration of the analytical method disclosed in Wittwer, wherein the negative signals are below the confidence band and positive signals are above the confidence band. In other word, Figure 5 does not contemplate, and thus does not teach or suggest to those of ordinary skill in the art, that positive and negative signals should always exhibit certain behavior. In addition, Figure 5 actually teaches away from the claimed invention because it shows that negative signals also exhibit a non-linear behavior.

Thus, the combination of Hall and Wittwer fails to teach or suggest the limitations of claims 1 and 15, which require determination of whether the transformed data set exhibits non-linear behavior and detection of target nucleotide if the transformed data set exhibits non-linear behavior. For this reason alone, the rejection of pending claims should be withdrawn.

The rejection of the claims is also based on columns 7 and 8 of Wittwer, which, together with Figure 5, allegedly disclose the steps (b) and (c) of claims 1 and 15. In reaching this conclusion, the Examiner appears to equate the determination of first and second derivatives disclosed in Wittwer with the transformation of data set (t, S(t)) as recited by the pending claims. Office Action, page 6. Applicants respectfully submit that such is not the case.

Contrary to the Examiner's allegation, the calculation of first and second derivatives in Wittwer does not provide the transformed data set (t*, S*(t*)), which can provide information whether the signals are positive or negative. *See* Wittwer, col. 8, lines 22-25 (referring to the calculated first and second derivatives as illustrated in Figure 7); *see, also, Id.*, Figure 7 (illustrating the use of first and second derivatives for the determination of baseline, but not for the determination of whether signals are positive or negative). Therefore, the first and second derivatives obtained in Wittwer are irrelevant in determining whether the signals exhibit linear or non-linear behavior, and thus whether the signals are positive or negative, as recited by the pending claims.

Despite this fact, the Examiner disregards Applicants' previous discussion on this point because "the entire issue and discussion regarding what Wittwer teaches fails [sic] to address itself to the claim." Office Action, page 8. Therefore, the Examiner contends, "when Applicant argues that the analysis is used, in part, to determine a background window, this does not distinguish the claimed invention." *Id.* Applicants respectfully submit that this assertion is incorrect.

The pending claims recite, in part, obtaining a data set (t, S(t)), transforming it to obtain (t*, S*(t*)), and determining whether the transformed data set exhibits non-linear behavior, wherein the target polynucleotide is detected if the transformed data set exhibits non-linear behavior. As such, Applicants fail to comprehend how the fact that the analytical method disclosed in Wittwer is directed to determining a background window is irrelevant to the pending claims. The pending claims clearly recite that: (1) a determination should be made as to whether the transformed data set exhibits non-linear behavior, which Wittwer fails to teach or suggest for the reasons stated above; and (2) the signals are positive where the transformed data set exhibits a non-linear behavior. In other words, the transformed data set recited by the pending claims is used directly to determine whether the signals are positive or not, which is a feature of claimed method properly recited by the pending claims. In contrast, the first and second derivatives disclosed in Wittwer are merely used for the determination of baseline window. Thus, the combination of Hall and Wittwer does not teach or suggest all of the claim limitations.

Apart from the fact that the combination of Hall and Wittwer does not teach or suggest all of the limitations of the claimed invention, no motivation existed prior to this invention to even combine the two. The Examiner disagrees, pointing to the portions of Wittwer that state that its algorithms are applicable to other amplification systems. However, as Applicants pointed out in their previous response, that portion of Wittwer refers to other PCR platforms, rather than to other amplification methods. *See* Wittwer, col. 5, lines 46-49.

In sum, Wittwer discloses "methods for automating detection [of] nucleic acids with real time PCR." Wittwer, col. 5, lines 45-46 (emphasis added). There is no teaching or suggestion in Wittwer that the methods disclosed in it can be used for any other methods than PCR. However, the claimed invention does not use PCR. *See, e.g*, the specification, page 1, lines 8-12 ("one of [various new assay techniques for detecting specific nucleic acid sequences], referred to as ...invasion assay, does not require the use of PCR."). As Applicants stated in their previous response, the background problem associated with an invasion assay is unique to that specific type of assay. Therefore, Applicants respectfully

submit that the combination of Hall and Wittwer fails to provide the required motivation or suggestion to combine those two references.

For at least the foregoing reasons, Applicants respectfully submit that the pending claims are allowable, and request that the rejection of the claims under 35 U.S.C. § 103 be withdrawn.

No fee is believed due for this response. However, if a fee is required for the submission of this paper, or to avoid the abandonment of this application, please charge such fee to Jones Day Deposit Account No. 503013. A copy of this sheet is enclosed.

Respectfully submitted,

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